

Applicants : Betty A. Diamond and Bruce T. Volpe
Appn. No. : 10/574,994
Filing Date January 31, 2007
Page 2 of 10

Amendments to the Specification:

Please enter the Sequence Listing attached hereto in both computer readable form on floppy disk and in paper form (1 page) (**Exhibit 2**) as the Sequence Listing for the subject application.

Please amend the paragraph on page 7, lines 1-7 as follows:

Thus, in some embodiments, the invention is directed to methods of preventing binding of an anti-double stranded (ds)-DNA antibody to a neuron in a mammal exhibiting or at risk for lupus-induced cognitive dysfunction. The anti-ds-DNA antibody in this method binds to an NR2 subunit of an NMDA receptor on the neuron. The methods comprise treating the mammal with at least one peptide or mimetic in an amount effective to bind to the antibody, where the peptide or mimetic comprises an amino acid sequence of X1-Trp-X1-Tyr-X2 (SEQ ID NO:1), wherein X1 represents Asp or Glu, and X2 represents Gly or Ser.

Please amend the paragraph on page 7, lines 8-14 as follows:

In other embodiments, the present invention is directed to methods of inhibiting progression of cognitive dysfunction in a mammal exhibiting or at risk for lupus-induced cognitive dysfunction. The methods comprise treating the mammal with at least one peptide or mimetic in an amount effective to bind to anti-ds-DNA antibodies that bind to an NR2 subunit of an NMDA receptor on a neuron. In these methods, the peptide or mimetic comprises an amino acid sequence of X1-Trp-X1-Tyr-X2 (SEQ ID NO:1), where X1 represents Asp or Glu, and X2 represents Gly or Ser.

Applicants : Betty A. Diamond and Bruce T. Volpe
Appn. No. : 10/574,994
Filing Date January 31, 2007
Page 3 of 10

Please amend the paragraph on page 10, lines 14-20 as follows:

Thus, in some embodiments, the invention is directed to methods of preventing binding of an anti-double stranded (ds)-DNA antibody to a neuron in a mammal exhibiting or at risk for lupus-induced cognitive dysfunction. In these embodiments, the anti-ds-DNA antibody binds to an NR2 subunit of an NMDA receptor on the neuron. The methods comprise treating the mammal with at least one peptide or mimetic in an amount effective to bind to the antibody, where the peptide or mimetic comprises an amino acid sequence of X1-Trp-X1-Tyr-X2 (SEQ ID NO:1), wherein X1 represents Asp or Glu, and X2 represents Gly or Ser.

Please amend the paragraph on page 10, lines 27-32 as follows:

The peptide or mimetic can be any length, provided the X1-Trp-X1-Tyr-X2 (SEQ ID NO:1) moiety is sufficiently exposed to bind to the anti-ds-DNA antibody binding site. In preferred embodiments, the peptide or mimetic is 5-30 amino acids in length. In more preferred embodiments, the peptide or mimetic is 5-10 amino acids in length. In the most preferred embodiments, the peptide or mimetic is 5 amino acids in length. The most preferred peptide or mimetic comprises Asp-Trp-Glu-Tyr-Ser (SEQ ID NO:1).

Please amend the paragraph on page 12, line 34 to page 13, line 5 as follows:

In other embodiments, the present invention is directed to methods of inhibiting progression of cognitive dysfunction in a mammal exhibiting or at risk for lupus-induced cognitive dysfunction. The methods comprise treating the mammal with at least one peptide or mimetic in an amount effective to bind to anti-ds-DNA antibodies that bind to an NR2 subunit of an NMDA receptor on a neuron. In these embodiments, as in the embodiments described above, the peptide or mimetic comprises an amino acid sequence

Applicants : Betty A. Diamond and Bruce T. Volpe
Appn. No. : 10/574,994
Filing Date January 31, 2007
Page 4 of 10

of X1-Trp-X1-Tyr-X2 (SEQ ID NO:1), wherein X1 represents Asp or Glu, and X2 represents Gly or Ser.

Please amend the paragraph on page 13, lines 6-9 as follows:

As in the above-described embodiments, the mimetic can be any mimetic known in the art, but preferably comprises D-amino acids. The peptide or mimetic can also be any length, but is preferably 5-30 amino acids, more preferably 5-10 amino acids, and most preferably 5 amino acids in length. The most preferred peptide or mimetic comprises Asp-Trp-Glu-Tyr-Ser (SEQ ID NO:1).

Please amend the paragraph on page 13, lines 19-27 as follows:

These methods can be preceded with a determination of the risk for lupus-induced cognitive dysfunction, preferably by determining whether the mammal has anti-NR2 antibodies, where the presence of anti-NR2 antibodies indicates that the mammal is at risk for lupus-induced cognitive dysfunction. This determination preferably includes a test to determine whether the anti-NR2 antibodies have crossed the blood-brain barrier, preferably by testing the cerebrospinal fluid for the presence of anti-NR2 antibodies. These methods are not narrowly limited to any particular test for anti-NR2 antibodies, as several suitable tests are known. A preferred example is the ELISA described in the Example, where binding of antibodies to the DWEYS (SEQ ID NO:1) peptide is assayed.

Please amend the paragraph on page 15, lines 1-7 as follows:

In preferred embodiments, the DNA mimotope is an octamer on a polylysine backbone comprising the peptide or mimetic comprising the sequence X1-Trp-X1-Tyr-X2 (SEQ ID NO:1), wherein X1 represents Asp or Glu, and X2 represents Gly or Ser. As

Applicants : Betty A. Diamond and Bruce T. Volpe
Appn. No. : 10/574,994
Filing Date January 31, 2007
Page 5 of 10

described in the Example, this DNA mimotope induces anti-ds-DNA antibodies that bind to the NR2 subunit of an NMDA receptor, which is present on all neurons. More preferably, the peptide or mimetic comprises the sequence Asp-Trp-Glu-Tyr-Ser (SEQ ID NO:1). In the most preferred embodiments, the peptide or mimetic consists of the sequence Asp-Trp-Glu-Tyr-Ser (SEQ ID NO:1).

Please amend the paragraph on page 15, lines 18-22 as follows:

In preferred embodiments, the DNA mimotope is an octamer on a polylysine backbone comprising the peptide or mimetic comprising the sequence X1-Trp-X1-Tyr-X2 (SEQ ID NO:1), wherein X1 represents Asp or Glu, and X2 represents Gly or Ser. More preferably, the peptide or mimetic comprises the sequence Asp-Trp-Glu-Tyr-Ser (SEQ ID NO:1). In the most preferred embodiments, the peptide or mimetic consists of the sequence Asp-Trp-Glu-Tyr-Ser (SEQ ID NO:1).